Amendments to the Claims:

This listing of claims will replace all prior versions, and listings of claims in the application:

Listing of Claims:

1 (currently amended): A method of screening for the integration of a DNA construct into a target gene having expression in the same cell or tissue type as a promoter having restricted expression in a mouse, said method comprising:

(i) transforming a mouse ES cell with a first DNA construct encoding a first indicator component under the control of [[a]] said promoter ~~having restricted expression in a mouse~~;

(ii) transforming the cell of (i) or a descendent of the cell by operably integrating into the cell's genome, a second DNA construct comprising DNA encoding a second indicator component not operably linked to a transcription control element;

(iii) producing tissue or specialized cells from the cell of (ii); and

(iv) monitoring the tissue or specialized cells of (iii) for a detectable indicator resulting from both the first and second indicator components indicative of integration of the second DNA construct into [[a]] said target gene ~~having restricted expression~~.

2 (canceled)

3 (currently amended): The method of ~~claims~~ claim **1** wherein the first and second indicator components are inactive fragments or subunits of an enzyme which, when combined, provide an active enzyme detectable by its activity.

4 (previously presented): The method of claim **1** wherein the first and second indicator components are independently detectable or selectable, and the detectable indicator is the presence of both indicator components in a cell.

5 (previously presented): The method of claim **1** wherein the first and second indicator components react in a sequence of reactions which result in a detectable indicator.

6 (currently amended): The method of claim **1** which additionally comprises isolating DNA endogenous to the mouse ES cell or descendent thereof which flanks the second DNA construct integrated into [[a]] said target gene ~~having restricted expression~~.

7-8 (canceled)

9 (previously presented): A DNA construct comprising, in a 5' to 3' direction, a splice acceptor, a sequence encoding an inactive subunit or fragment of an enzyme and, an IRES wherein said sequence encoding the enzyme subunit or fragment is not operably linked to a transcription control element, and wherein said subunit or fragment is active when combined with a further subunit.

10-11 (canceled)

12 (previously presented): The combination of:

(i) a DNA construct for integration into the genome of an eukaryotic cell comprising a sequence encoding a first indicator component under the control of a promoter having restricted expression; and

(ii) a DNA construct for integration into the genome of a eukaryotic cell, comprising in the 5' to 3' direction, a splice acceptor, a sequence encoding a second indicator component not operably linked to a transcription control element, and an optional IRES, wherein expression of both the first and second indicator components in said cell is detectable, and wherein if said first indicator component is an antibiotic resistance marker, said second indicator component is not an antibiotic resistance marker.

13 (previously presented): A mouse ES cell or descendent thereof, transformed by the combination of DNA constructs of claim **12**.

14 (canceled)

15 (previously presented): A DNA construct comprising, in a 5' to 3' direction, a splice acceptor and a sequence encoding an inactive alpha or omega fragment of β-galactosidase, wherein said sequence encoding the inactive alpha or omega fragment is not operably linked to a transcription control element and said fragment is active when combined with another fragment of β-galactosidase.

16 (currently amended): A method of screening for the integration of a DNA construct into a target gene having expression in the same cell or tissue type as a promoter having restricted expression in a mouse, said method comprising:

(i) transforming a mouse ES cell with a first DNA construct encoding a first indicator component linked to [[a]] said promoter ~~having restricted expression in a mouse~~, wherein DNA encoding the first indicator component is separated from said promoter by a sequence of DNA which prevents transcriptional control by said promoter over the DNA encoding the first indicator component;

(ii) transforming the cell of (i) or a descendent of the cell by operably integrating into the cell's genome, a second DNA construct comprising DNA encoding a second indicator component not operably linked to a transcription control element;

(iii) producing tissue or specialized cells of (ii); and

(iv) monitoring the tissue or specialized cells of (iii) for a detectable indicator resulting from both the first and second indicator components indicative of integration of the second DNA construct into [[a]] said target gene ~~having restricted expression~~, wherein in the second DNA construct, the second indicator component is a recombinase capable of removing the sequence of DNA preventing transcriptional control in the first DNA construct; and,

wherein said monitoring is for cells in which the first indicator component is expressed under the transcriptional control of the promoter having restricted expression.

17 (previously presented): The method of claim **16** wherein the DNA preventing transcriptional control is flanked by lox sites and the recombinase is Cre.

18 (currently amended): A method of producing mouse tissue or specialized cells comprising a detectable indicator associated with a target gene having expression in the same cell or tissue type as a promoter having restricted expression in a mouse, which comprises:

(i) transforming a mouse ES cell with a first DNA construct encoding a first indicator component under the control of [[a]] said promoter ~~having restricted expression in a mouse~~;

(ii) transforming the cell of (i) or a descendent of the cell by integrating into the cell's genome, a second DNA construct comprising DNA encoding a second indicator component not operably linked to a transcription control element;

(iii) producing tissue or specialized cells from the cell of (ii); and

(iv) selecting tissue or specialized cells of (iii) by the presence of a detectable indicator resulting from both the first and second indicator components.

19 (currently amended): A method of producing a mouse comprising a detectable indicator associated with a target gene having expression in the same cell or tissue type as a promoter having restricted expression in a mouse, which comprises:

(i) transforming a mouse ES cell by integrating into the cell's genome, a first DNA construct encoding a first indicator component under the control of [[a]] said promoter ~~having restricted expression~~;

(ii) transforming the cell of (i) or a descendent of the cell by integrating into the cell's genome, a second DNA construct comprising DNA encoding a second indicator component not operably linked to a transcription control element;

(iii) selecting transformed cells of (ii);

(iv) introducing selected cells of (iii) into a mouse host embryo;

(v) implanting the host embryo of (iv) into a pseudopregnant mouse;

(vi) maintaining the mouse of (v) while offspring develops to term from the host embryo; and

(vii) selecting offspring of (vi) by the presence of a detectable indicator resulting from both the first and second indicator components in tissue or specialized cells of the offspring.